

Prospective study on metabolic and hormonal disorders in patients with polycystic ovary syndrome with or without thyroid involvement

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Abstract:
Introduction: Polycystic ovary syndrome (PCOS) is an endocrine condition with complex metabolic implications. The aim of the study was to compare the biomarker and clinical characteristics of patients diagnosed with PCOS, with or without thyroid dysfunction, in comparison with those of patients without PCOS and to analyze their association with the risk of developing PCOS.
Materials and Methods: We conducted a prospective observational study that included 120 patients. The data were analyzed descriptively and through logistic regressions to identify the association between PCOS and metabolic disorders, as well as their association with thyroid status. We reported the results of the regressions as relative risk ratios (RRR) or standardized beta coefficients and 95% confidence intervals (CI).
Results: Among all the parameters analyzed, cholesterol had a strong positive association with the occurrence of both hypothyroidism and hyperthyroidism. PCOS was significantly associated with body mass index values, luteinizing hormone, testosterone, total serum cholesterol, fasting glucose, HOMA index (Homeostatic Model Assessment for Insulin Resistance), and waist circumference.
Conclusions: Early identification of metabolic abnormalities in patients with PCOS can facilitate lifestyle changes and pharmacological treatments, improving both their reproductive health and overall metabolic profiles.

Keywords: polycystic ovary syndrome; metabolic disorders; hypothyroidism; hyperthyroidism.

Introduction

Polycystic Ovary Syndrome (PCOS) is a common endocrine condition that affects a significant proportion of reproductive-aged women, characterized by a multitude of manifestations, including oligomenorrhea, hyperandrogenism, and the polycystic appearance of the ovaries on ultrasound examination (1). In addition to its reproductive implications, an increasing body of evidence suggests that PCOS is a complex metabolic condition that predisposes affected patients to an increased risk of cardiovascular diseases and type 2 diabetes (2, 3).

Metabolic syndrome includes a broad range of metabolic disorders characterized by

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abdominal obesity, insulin resistance, hypertension, and dyslipidemia (4). Patients with PCOS frequently exhibit insulin resistance, which not only plays an essential role in the pathophysiology of the syndrome, but also exacerbates the risk of developing metabolic syndrome (5, 6).

The high prevalence of obesity among women with PCOS further complicates this relationship, leading to a vicious cycle that increases the likelihood of adverse metabolic outcomes (7).

A cross-sectional study assessed the prevalence of metabolic syndrome based on PCOS phenotypes in a cohort of 111 patients (8). In the cited study, the overall prevalence of metabolic syndrome was 33.6% and did not show statistically significant differences between the four phenotypes regarding the prevalence of metabolic syndrome.

However, phenotype D exhibited a significantly higher mean fasting glucose level, as well as a significantly lower mean HDL cholesterol level compared to the other phenotypes (8). Patients in this group had a high prevalence of abdominal circumference ≥ 80 cm (68.2%), as well as the highest average abdominal circumference (90.1 cm) (8). Among patients with an abdominal circumference ≥ 80 cm, phenotype A increased the chances of developing metabolic syndrome approximately six-fold compared to phenotype C.

Last but not least, an observational case-control study that included a total of 526 reproductive-aged patients compared metabolic parameters and insulin resistance among the four phenotypes of PCOS defined according to the Rotterdam criteria and determined predictors of these complications (9). Insulin resistance was identified in 42.6% of patients with PCOS. There were no significant

differences in the frequency of insulin resistance and metabolic syndrome among the four PCOS phenotypes (9). The Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) index ≥ 3.8 was the most common predictor of insulin resistance in patients with PCOS.

This complex interaction between PCOS and metabolic syndrome necessitates a comprehensive approach that incorporates both endocrine and metabolic evaluations, highlighting the importance of multidisciplinary care in optimizing health outcomes for affected women. In this observational prospective study, we compared the biomarker and clinical characteristics of patients diagnosed with PCOS, with or without metabolic involvement, in comparison with those of patients without PCOS and analyzed their association with the risk of developing PCOS.

Materials and methods

This prospective observational study included 120 patients who were evaluated at the Endocrinology Clinic of "Saint Spiridon" Hospital in Iași, between January 1, 2022, and March 31, 2024. Ethical approval for conducting this study was obtained from the Research Ethics Committee of the "Grigore T. Popa" University of Medicine and Pharmacy in Iași (No. 132/14.12.2021).

The study included patients with or without PCOS, with or without thyroid dysfunction, who were at least 18 years old and had given their consent for monitoring. Patients were excluded from this study if they: were minors, had idiopathic hirsutism, hyperprolactinemia, congenital adrenal hyperplasia, androgen-producing tumors, Cushing's disease, incomplete medical records, were pregnant or postpartum and could not provide informed consent.

Patients were followed according to standard protocol, and the medical data from their records were analyzed to identify the following clinical and paraclinical parameters: diagnosis of PCOS, thyroid status, classification within the PCOS phenotype, age, environment, body mass index, serum values of follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, sex hormone binding globulin (SHBG), dehydroepiandrosterone sulfate (DHEAS), lipid profile: total cholesterol, high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol, fasting glucose, HOMA-IR score, abdominal circumference.

The medical data were analyzed descriptively. We used descriptive statistics and compared categorical variables using the Pearson χ^2 test and continuous variables using the Student's t-test or ANOVA between our groups.

A p-value less than 0.05 was considered statistically significant. These analyses were performed using STATA SE (version 17, 2023, StataCorp LLC, College Station, TX, USA). Violin plots were used to illustrate the comparisons between numerical parameters across groups.

Additionally, we performed multinomial logistic regression to identify the association between PCOS and metabolic disorders, as well as the association of these metabolic disorders with each other. We reported the results as relative risk ratios (RRRs) and 95% confidence intervals (CI). The model was adjusted for the patients' age.

Finally, we performed a logistic regression to assess the association between numerical parameters, the presence of PCOS, and thyroid status in the evaluated cohort, and the results were reported as standardized beta coefficients and 95%CI.

Results

This study included 120 patients whose data were recorded prospectively. A graphical representation of the age comparison between the main study groups is shown in Figure 8.1. The mean age and standard deviation for the PCOS patient group was 32.74 ± 12.86 years, while the mean age and standard deviation for the control group was 30.85 ± 10.01 years. The median age for the first analyzed group was 30 years (interquartile range, IQR: 19-71), and for the second group, it was 19 years (IQR: 19-53).

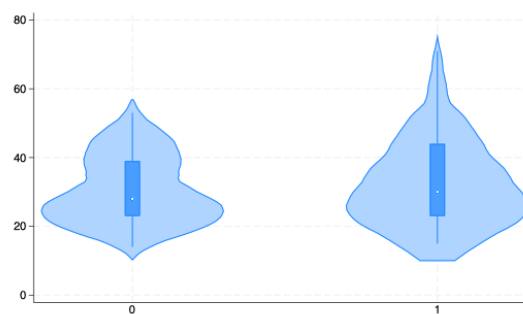


Figure 1. Violin plot showing age comparison by study groups. Legend: 1 – PCOS group, 0 – control group.

Most of the patients lived in urban areas, and this aspect was confirmed for both the PCOS group (55.93%) and for the control group (67.21%). A comparative presentation of the BMI values between the two groups is shown in Figure 2. The median BMI value for the first evaluated group was 24 kg/m^2 (IQR: 21-27), while for the second group it was 22 kg/m^2 (IQR: 20-25). The corresponding values for the distribution skewness were 0.23 and 1, while the kurtosis values were 2.25 and 4.88. The mean value and standard deviation of BMI for the PCOS-affected patient group were $24.13 \pm 3.48 \text{ kg/m}^2$, while for the control group it was $22.73 \pm 3.27 \text{ kg/m}^2$.

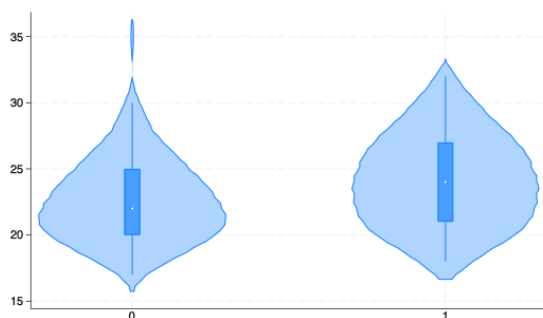


Figure 2. Violin plot showing the comparison of BMI by study groups. Legend: 1 – PCOS group, 0 – control group.

A comparative analysis using ANOVA and the Bonferroni post-hoc test of numerical parameters based on thyroid status and the presence or absence of PCOS is presented in Table 1.

The mean value and standard deviation for FSH were significantly lower in patients with PCOS and hypothyroidism compared to those with PCOS and without hypothyroidism (4.58 ± 1.21 versus 5.70 ± 0.63 UI/L, $p = 0.01$).

On the other hand, the mean value and standard deviation for LH were significantly higher in patients with PCOS and hypothyroidism compared to those with PCOS and without hypothyroidism (9.73 ± 4.72 versus 5.25 ± 2.75 UI/L, $p = 0.01$), and the trend was maintained for patients with PCOS and hyperthyroidism (11.82 ± 5.63 versus 5.66 ± 3.88 UI/L, $p = 0.01$).

The serum level of SHBG was significantly lower for patients with PCOS

affected by hypothyroidism (31 ± 19.25 versus 56.6 ± 29.00 nmol/L, $p = 0.01$) or hyperthyroidism (33.7 ± 22.51 versus 64 ± 31.88 nmol/L, $p = 0.02$) compared to the controls.

The serum testosterone level was significantly higher in patients with PCOS and hypothyroidism (53.82 ± 25.28 versus 27.7 ± 10.25 ng/dl, $p = 0.04$), while the serum level of DHEAS was higher in patients with PCOS and hyperthyroidism (6.25 ± 1.72 versus 4.24 ± 2.17 ng/ml, $p = 0.03$) compared to the controls.

The serum cholesterol level was significantly higher among patients with hypothyroidism (292.23 ± 11.03 versus 208.75 ± 41.39 mg/dl, $p < 0.001$), hyperthyroidism (296.4 ± 17.97 versus 194.77 ± 14.80 mg/dl, $p < 0.001$) or euthyroidism (290.84 ± 12.39 versus 196.28 ± 19.13 mg/dl, $p < 0.001$) compared to the controls.

The same observation was confirmed for fasting glucose, which had a significantly higher serum level among patients with hypothyroidism (91.82 ± 9.00 versus 84.7 ± 6.51 mg/dl, $p = 0.03$), hyperthyroidism (96 ± 12.39 versus 83 ± 7.01 mg/dl, $p = 0.01$), or euthyroidism (95.87 ± 11.23 versus 84.90 ± 7.35 mg/dl, $p < 0.001$) compared to the controls.

Last but not least, the HOMA index was significantly higher among patients with hypothyroidism (5.06 ± 2.77 versus 2.17 ± 1.00 , $p = 0.004$) and hyperthyroidism (4.41 ± 2.36 versus 2.31 ± 1.25 , $p = 0.02$) compared to the controls.

Table I. The results of the ANOVA analysis and the Bonferroni post-hoc test to evaluate the association between numerical parameters, PCOS, and thyroid status in the studied cohort.

Numerical Parameter	PCOS vs. Control			PCOS vs. Control			PCOS vs. Control		
	Hypothyroidism		p	Hyperthyroidism		p	Euthyroidism		p
	Mean and SD	Mean and SD		Mean and SD	Mean and SD		Mean and SD	Mean and SD	

BMI (kg/m ²)	24.70± 2.97	25± 2.94	0.80	23.7± 4.16	24.88± 5.27	0.59	23.96± 3.58	21.73± 2.24	0.001
FSH (UI/L)	4.58± 1.21	5.70± 0.63	0.01	5.39± 1.10	6.07± 1.30	0.23	5.41± 1.20	5.62± 1.22	0.45
LH (UI/L)	9.73± 4.72	5.25± 2.75	0.01	11.82± 5.63	5.66± 3.88	0.01	12.75± 7.59	6.23± 3.21	<0.00 1
Testosterone (ng/dl)	53.82± 25.28	27.7± 10.25	0.04	47.3± 23.5	35.22± 14.86	0.20	52.25± 21.80	34.35± 19.36	0.0004
SHBG (nmol/L)	31± 19.25	56.6± 29.00	0.01	33.7± 22.51	64± 31.88	0.02	34.87± 19.61	65.5± 28.15	<0.00 1
DHEAS (ng/ml)	6.38± 1.87	4.86± 2.74	0.09	6.25± 1.72	4.24± 2.17	0.03	7.12± 1.30	4.74± 2.90	0.0001
Cholesterol (mg/dl)	292.23 ± 11.03	208.75 ± 41.39	<0.00 1	296.4± 17.97	194.77 ± 14.80	<0.00 1	290.84 ± 12.39	196.28 ± 19.13	<0.00 1
HDL (mg/dl)	49.82± 16.05	56.8± 15.15	0.27	51.5± 22.55	61.33± 19.18	0.32	47.28± 16.39	56.80± 20.66	0.03
LDL (mg/dl)	103± 31.28	104.9± 25.09	0.45	112.3± 29.07	113.55 ± 34.11	0.93	110.71 ± 34.21	102.16 ± 31.24	0.26
TG (mg/dl)	123.05 ± 80.84	115.7± 35.79	0.78	69.3± 34.40	89.44± 41.32	0.26	86.96± 60.58	115.5± 65.56	0.05
Fasting glucose (mg/dl)	91.82± 9.00	84.7± 6.51	0.03	96± 12.39	83± 7.01	0.01	95.87± 11.23	84.90± 7.35	<0.00 1
HOMA	5.06± 2.77	2.17± 1.00	0.004	4.41± 2.36	2.31± 1.25	0.02	4.37± 2.48	2.79± 1.42	<0.00 1
WC (cm)	100.11 ± 18.46	89.3± 5.41	0.08	103.3± 16.77	86.66± 5.89	0.01	97.59± 14.05	89.19± 6.78	0.001

Legend: SD - standard deviation, FSH - follicle-stimulating hormone, LH - luteinizing hormone, SHBG - sex hormone-binding globulin, DHEAS - dehydroepiandrosterone sulfate, HDL - high-density lipoprotein, LDL - low-density lipoprotein, WC - waist circumference, TG - triglycerides, BMI - body mass index.

The analysis of correlations between the presence of PCOS, hormonal parameters, and BMI is shown in Table II.

Table II. Analysis of the correlations between the presence of PCOS, hormonal parameters, and BMI

Correlations	Group	BMI	FSH	LH	Testosterone	SHBG	DHEAS
Group	1.0000						
BMI	0.2042	1.0000					
	0.5307						
FSH	-0.2195	-0.0261	1.0000				
	0.3361						
LH	0.4884	-0.0323	0.0528	1.0000			
	0.0000						
Testosterone	0.4167	0.1148	-0.0440	0.2205	1.0000		
	0.0000			0.3258			
SHBG	-0.5270	-0.0479	0.0462	-0.2546	-0.0762	1.0000	
	0.0000			0.1051	1.0000		
DHEAS	0.4210	0.0999	-0.0960	0.2662	0.2407	-0.3214	1.0000
	0.0000			0.0691	0.1697	0.0072	

Legend: FSH - follicle-stimulating hormone, LH - luteinizing hormone, SHBG - sex hormone-binding globulin, DHEAS - dehydroepiandrosterone sulfate, BMI - body mass index.

Our results indicated that the presence of PCOS was positively and significantly correlated with LH levels ($\rho = 0.48$, $p < 0.001$), total serum testosterone ($\rho = 0.41$, $p < 0.001$), and DHEAS ($\rho = 0.42$, $p < 0.001$). These correlations were moderate.

We also identified negative and significant correlations between the presence of PCOS and serum SHBG levels ($\rho = -0.52$, $p < 0.001$), as

well as between DHEAS levels and SHBG ($\rho = -0.32$, $p = 0.007$). These correlations were moderate and small.

The analysis of correlations between the presence of PCOS, lipid profile parameters, glucose levels, HOMA index, waist circumference, and BMI is shown in Table III.

Table III. Analysis of the correlations between the presence of PCOS, BMI, lipid profile parameters, glucose levels, HOMA index, and waist circumference.

Correlations	Group	BMI	Cholesterol	HDL	LDL	Glucose	HOMA	WC
Group	1.0000							
BMI	0.2042	1.0000						
	0.7075							
Cholesterol	0.9271	0.1843	1.0000					
	0.0000	1.0000						

HDL	- 0.2332	- 0.1090	-0.2063	1.0000				
	0.2902	1.0000	0.6661					
LDL	0.0715	- 0.0432	0.0668	0.1357	1.0000			
	1.0000	1.0000	1.0000	1.0000				
Glucose	0.4890	0.0591	0.4559	- 0.0650	0.0392	1.0000		
	0.0000	1.0000	0.0000	1.0000	1.0000			
HOMA	0.4405	0.0639	0.4302	- 0.1418	0.0344	0.2138	1.0000	
	0.0000	1.0000	0.0000	1.0000	1.0000	0.5330	0.3641	
WC	0.4034	0.2021	0.3776	- 0.0373	-0.0106	0.2768	0.2262	1.0000
	0.0001	0.7510	0.0006	1.0000	1.0000	0.0619	0.3641	

Legend: BMI - body mass index, HDL - high-density lipoprotein, LDL - low-density lipoprotein, WC - waist circumference, TG – triglycerides.

The strongest and most significant correlation was established between the presence of PCOS and the level of total serum cholesterol ($\rho = 0.92$, $p < 0.001$).

Additionally, we identified moderate positive correlations between the presence of PCOS and fasting glucose levels ($\rho = 0.48$, $p < 0.001$), the HOMA index ($\rho = 0.44$, $p < 0.001$), and waist circumference ($\rho = 0.40$, $p < 0.001$).

The level of total serum cholesterol was significantly positively correlated with fasting glucose levels ($\rho = 0.45$, $p < 0.001$), the HOMA index ($\rho = 0.43$, $p < 0.001$), and waist circumference ($\rho = 0.37$, $p < 0.001$).

We performed a multinomial regression to assess the association between numerical

parameters and PCOS in the evaluated cohort, and the results are presented in Table IV.

Among all the parameters analyzed, PCOS was significantly associated with BMI value (RRR: 1.22, 95% CI: 1-1.48, $p = 0.04$), LH levels (RRR: 1.31, 95% CI: 1.13-1.52, $p < 0.001$), total serum testosterone levels (RRR: 1.06, 95% CI: 1.02-1.10, $p = 0.004$), SHBG levels (RRR: 0.93, 95% CI: 0.90-0.97, $p < 0.001$), total cholesterol level (RRR: 1.11, 95% CI: 1.06-1.16, $p < 0.001$), fasting glucose levels (RRR: 1.13, 95% CI: 1.06-1.21, $p < 0.001$), HOMA index (RRR: 1.68, 95% CI: 1.29-2.19, $p = 0.03$), and waist circumference (RRR: 1.07, 95% CI: 1.02-1.11, $p = 0.003$).

Table IV. Multinomial logistic regression to assess the association between numerical parameters and PCOS in the evaluated cohort.

Group	RRR	Standard error	z	P value	[95% CI]
BMI	1.22	0.12	1.99	0.046	[1.00, 1.48]
FSH	0.49	0.14	2.48	0.013	[0.28, 0.86]
LH	1.31	0.10	3.50	0.000	[1.13, 1.52]
Testosterone	1.06	0.02	2.86	0.004	[1.02, 1.10]
SHBG	0.93	0.02	3.91	0.000	[0.90, 0.97]
DHEAS	1.27	0.19	1.64	0.102	[0.95, 1.70]
Cholesterol	1.11	0.03	4.22	0.000	[1.06, 1.16]
HDL	1.03	0.03	0.85	0.396	[0.97, 1.09]
LDL	0.99	0.02	-0.22	0.823	[0.96, 1.03]
TG	0.99	0.01	-0.15	0.884	[0.98, 1.02]
Fasting glucose	1.13	0.04	3.83	0.000	[1.06, 1.21]
HOMA	1.68	0.23	3.83	0.000	[1.29, 2.19]
WC	1.07	0.02	2.94	0.003	[1.02, 1.11]

Legend: RRR- relative risk ratio, CI -confidence interval, FSH - follicle-stimulating hormone, LH - luteinizing hormone, SHBG - sex hormone-binding globulin, DHEAS - dehydroepiandrosterone sulfate, BMI - body mass index, HDL - high-density lipoprotein, LDL - low-density lipoprotein, WC - waist circumference, TG – triglycerides.

Finally, we performed a logistic regression to assess the association between numerical parameters, the presence of PCOS, and thyroid status in the evaluated cohort, and the results are presented in Table V.

Among all the parameters analyzed, cholesterol had a strong positive association with the occurrence of both hypothyroidism and

hyperthyroidism. Therefore, the standardized beta coefficient for this parameter in the case of hypothyroidism was 0.70, which means that for each one standard deviation increase in its value, we expect the risk of hypothyroidism in the context of PCOS to increase by 0.70 standard deviations ($p < 0.001$).

Similarly, the standardized beta coefficient for this parameter in the case of

hyperthyroidism was 0.80, which means that for each one standard deviation increase in its value, we expect the risk of hyperthyroidism in the context of PCOS to increase by 0.80 standard deviations ($p < 0.001$).

At the same time, the serum level of fasting glucose was strongly associated with hypothyroidism, but not with hyperthyroidism. Thus, the standardized beta coefficient for this parameter in the case of hypothyroidism was 1.13, which means that for each one standard deviation increase in its value, we expect the risk of hypothyroidism in the context of PCOS to increase by 1.13 standard deviations ($p = 0.04$).

The serum level of testosterone was also strongly associated with hypothyroidism, but not with hyperthyroidism. Therefore, the standardized beta coefficient for this parameter in the case of hypothyroidism was 0.46, which means that for each one standard deviation increase in its value, we expect the risk of hypothyroidism in the context of PCOS to increase by 0.46 standard deviations ($p = 0.001$).

A similar situation was found for the serum level of LH, whose standardized beta

coefficient was 0.29 for this parameter in the case of hypothyroidism, indicating that for each one standard deviation increase in its value, we expect the risk of hypothyroidism in the context of PCOS to increase by 0.29 standard deviations ($p = 0.019$). In this case, the magnitude of the association was weaker.

On the other hand, the serum levels of FSH and SHBG showed a moderate negative association with the occurrence of hypothyroidism in the context of PCOS. Thus, the standardized beta coefficient for FSH in the case of hypothyroidism was -0.34, meaning that for each one standard deviation increase in its value, we expect the risk of hypothyroidism in the context of PCOS to decrease by 0.34 standard deviations ($p = 0.008$).

Additionally, the standardized beta coefficient was -0.35 for SHBG in the case of hypothyroidism, which means that for each one standard deviation increase in its value, we expect the risk of hypothyroidism in the context of PCOS to decrease by 0.35 standard deviations ($p = 0.006$).

Table V. Logistic regression to assess the association between numerical parameters, PCOS, and the presence of hypothyroidism in the evaluated cohort.

Hypothyroidism	Standardized Beta Coefficient	P value	Hyperthyroidism	Coefficient Beta standardizat	P value
BMI	-0.04	0.80	BMI	-0.13	0.59
FSH	-0.34	0.008	FSH	-0.15	0.43
LH	0.29	0.019	LH	-0.36	0.14
Testosterone	0.46	0.001	Testosterone	.012	0.56

SHBG	-0.35	0.006	SHBG	-0.35	0.14
DHEAS	0.07	0.59	DHEAS	0.15	0.51
Cholesterol	0.70	<0.001	Cholesterol	0.80	<0.001
HDL	0.003	0.97	HDL	-0.18	0.10
LDL	-0.08	0.45	LDL	0.07	0.47
TG	0.10	0.40	TG	0.01	0.83
Fasting glucose	1.13	0.04	Fasting glucose	0.05	0.58
HOMA	0.20	0.11	HOMA	0.08	0.46
WC	0.13	0.30	WC	0.11	0.37

Legend: FSH - follicle-stimulating hormone, LH - luteinizing hormone, SHBG - sex hormone-binding globulin, DHEAS - dehydroepiandrosterone sulfate, BMI - body mass index, HDL - high-density lipoprotein, LDL - low-density lipoprotein, WC - waist circumference, TG – triglycerides.

Discussion

Understanding the associations between PCOS and metabolic syndrome is crucial for developing effective screening and intervention strategies aimed at reducing long-term health risks.

Our results showed that patients with PCOS and hypothyroidism exhibited significantly higher values of LH, DHEAS, total cholesterol, blood glucose, HOMA index, and abdominal circumference compared to the control group. On the other hand, serum levels of FSH and SHBG were significantly lower for patients with PCOS affected by hypothyroidism.

Patients with PCOS and hyperthyroidism showed significantly higher values of LH, serum testosterone, DHEAS, total cholesterol, blood glucose, HOMA index, and abdominal circumference compared to the control group. Serum SHBG levels were significantly lower compared to the control group. Among all analyzed parameters, cholesterol had a positive and strong association with both the occurrence of hypothyroidism and hyperthyroidism. Additionally, serum levels of fasting blood glucose, testosterone, and LH were strongly associated with hypothyroidism but not with hyperthyroidism. Conversely, serum levels of FSH and SHBG showed a moderate and negative

association with the occurrence of hypothyroidism in the context of PCOS.

PCOS was significantly associated with BMI value, LH levels, total serum testosterone levels, SHBG levels, total cholesterol levels, fasting blood glucose levels, HOMA index, and abdominal circumference.

Our results are in agreement with previously published data in the literature. Thus, Trummer and colleagues analyzed the impact of elevated TSH levels on metabolic and endocrine phenotypes in 583 patients diagnosed with PCOS (10). Endocrine and metabolic parameters were measured in all patients and compared between those with and without elevated TSH levels.

The authors showed that patients with elevated TSH levels had significantly higher basal insulin levels, HOMA index, and total cholesterol/ HDL ratio, while free thyroxine and HDL levels were significantly lower compared to the control group (10). Women with PCOS and euthyroid status under thyroid hormone replacement therapy displayed significant differences regarding TSH levels, age, body mass index, HDL, and systolic blood pressure compared to those without hormone replacement therapy (10).

Yue and colleagues conducted a prospective study analyzing associations between subclinical hypothyroidism and endocrine metabolic characteristics in 321 patients diagnosed with PCOS (11). The authors showed that in patients with PCOS with normal FT4 levels, those with $TSH \geq 4.2$ mU/L had higher prolactin levels, an increased LH/FSH ratio, and a significantly higher visceral fat index.

In the cited study, total triglyceride levels were significantly higher, while total HDL cholesterol levels were significantly lower in patients with $TSH \geq 4.2$ mU/L compared to those with $TSH < 4.2$ mU/L (11). Additionally, in patients with PCOS and normal FT4, those with $TSH \geq 2.5$ mU/L had

significantly higher values of body mass index, prolactin, triglycerides, and visceral fat index, as well as significantly lower values of HDL cholesterol compared to patients with $TSH < 2.5$ mU/L (11).

A meta-analysis conducted by de Medeiros and colleagues investigated the impact of subclinical hypothyroidism on the characteristics of patients with PCOS by analyzing data from 9 selected studies that included a total of 1,537 patients with PCOS and euthyroid status and 301 patients with PCOS and subclinical hypothyroidism (12).

The results of the meta-analysis showed that anthropometric parameters were similar between the analyzed groups (12). Total cholesterol and triglyceride levels were significantly higher in the group of patients with PCOS and subclinical hypothyroidism. Additionally, HDL-C cholesterol was lower in the group of patients with PCOS and subclinical hypothyroidism. Fasting blood glucose was significantly lower in patients with PCOS and euthyroid status. At the same time, androgen levels were similar in both analyzed groups.

Therefore, it is important to pay attention to subclinical hypothyroidism, which can be associated with endocrine abnormalities, dyslipidemia, and visceral obesity in patients diagnosed with PCOS.

Moreover, patients diagnosed with PCOS who experience persistent anovulation despite lifestyle modifications and medical therapy can benefit from ovarian drilling. This minimally invasive surgical procedure aims to reduce androgen levels, restore ovulatory function, and improve fertility outcomes in women with PCOS and infertility (13). In cases where pharmacological treatments, such as clomiphene citrate, have proven ineffective after multiple cycles, ovarian drilling can provide an alternative pathway to enhance ovarian function.

It is important to consider certain limitations when interpreting the results of this study. Limitations of this study include the relatively small sample size of patients, inclusion of a limited number of clinical and paraclinical factors, and the presence of unbalanced datasets.

Conclusions

Understanding the associations between PCOS and metabolic syndrome is crucial for developing effective screening and intervention strategies aimed at reducing long-term health risks. Early identification of metabolic abnormalities in patients with PCOS can facilitate lifestyle modifications and pharmacological treatments, improving both reproductive health and overall metabolic profiles. This intricate interplay between PCOS and metabolic syndrome necessitates a comprehensive approach that incorporates both endocrine and metabolic evaluations, underscoring the importance of multidisciplinary care in optimizing health outcomes for affected women.

Abbreviations

1. BMI - Body Mass Index
2. DHEAS - Dehydroepiandrosterone Sulfate
3. FSH - Follicle-Stimulating Hormone
4. FT4 - Free Thyroxine
5. HDL - High-Density Lipoprotein
6. HOMA - Homeostatic Model Assessment
7. HOMA - Homeostatic Model Assessment for Insulin Resistance
8. LH - Luteinizing Hormone
9. LDL - Low-Density Lipoprotein
10. PCOS - Polycystic Ovary Syndrome
11. SHBG - Sex Hormone-Binding Globulin
12. TG - Triglycerides
13. TSH - Thyroid-Stimulating Hormone

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Competing Interests

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

Conflicts of Interest and Source of Funding

All the authors declare no funding received and no conflict of interest.

Ethics approval and Consent to Participate

The authors confirm that all the procedures were followed in accordance with the relevant guidelines of the Helsinki declaration. Ethical approval for conducting this study was obtained from the Research Ethics Committee of the "Grigore T. Popa" University of Medicine and Pharmacy in Iași (No. 132/14.12.2021).

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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